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### **Excess cancer incidence among workers exposed to fluoride.**

by [Grandjean P](#), [Olsen JH](#), [Juel K](#)

**Affiliation:** Institute of Community Health, Odense University, Denmark.

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## Excess cancer incidence among workers exposed to fluoride<sup>1</sup>

by Philippe Grandjean, MD,<sup>2</sup> Jørgen H Olsen, MD,<sup>3</sup> Knud Juel, MS<sup>4</sup>

A recent bioassay has shown an increased frequency of bone cancer in rats with a high oral intake of fluoride, but the data were considered to represent equivocal evidence of carcinogenicity (1). Few data are available on the possible carcinogenicity of heavy occupational exposures to fluoride.

We have therefore extended our previous follow-up (2) of a cohort of 425 men and an additional group of 97 women employed for at least six months during 1924—1961 at the cryolite processing plant in Copenhagen. A full report of this study is being published elsewhere (3).

Fluoride exposures at the cryolite plant were considerable, and many workers developed serious skeletal fluorosis. The average daily fluoride absorption could be estimated to be about 35 mg (ie, more than 10-fold higher than the daily uptake in communities with water fluoridation).

Mortality was recorded during 1941—1989 and cancer morbidity during 1943—1987. For comparison, we used national mortality rates and cancer incidence rates for the Copenhagen area.

A total of 300 deaths occurred among the men, while only 223 were expected. Cancer and violent death were responsible for most of this excess. However, the cardiovascular mortality was in accordance with the rates for Danish men in general.

A total of 119 cancer cases occurred among the male workers, as compared with 103.6 cases expected on the basis of the Copenhagen rates. Excesses were seen for cancer of the lungs [ $N = 35$ , standard incidence ratio (SIR) 1.35], larynx ( $N = 5$ , SIR 2.29), and urinary bladder ( $N = 17$ , SIR 1.84). Maximum morbidity occurred after 10—19 years of exposure, but the cancer incidence did not show any stable relationship with length of employment. The incidence

of respiratory and urinary cancers was particularly high among the men who were less than 35 years of age at first employment. Although bladder cancer occurred in two female workers (SIR 2.18), the number of cases among the women was too small to allow any detailed evaluation. Cancer of the bone (expected 0.2) was not observed in any cryolite worker. However, due to the small size of the cohort, a relative risk of up to 18 for this rare form of cancer could not be excluded.

The increased rates of respiratory cancer are probably caused by cigarette smoking, although a partial adjustment for tobacco smoking was achieved with the use of Copenhagen rates for comparison. However, the cardiovascular mortality was not increased and was even slightly below that expected for Copenhagen men. More importantly, the disproportionate increase in the incidence rate for bladder cancer is difficult to explain by smoking habits alone. Thus tobacco smoking would be likely to cause a three-fold higher excess in lung cancer than in bladder cancer (4). The pattern established for the cryolite workers was almost exactly the opposite.

Whether bladder cancer is a plausible effect of fluoride exposure is currently difficult to determine. About half of the absorbed fluoride is rapidly excreted into the urine and will therefore reach the epithelium of the urinary bladder. The evidence for genotoxicity is limited (1). With regard to bone cancer, the absence of this rare cancer in a small cohort is not surprising. However, in rats that showed increased risk of bone cancer in the bioassay (1), continued ossification occurred after the first year of life (ie, for about half of the exposure period) (5). In contrast, ossification would have been completed in the cryolite workers at the beginning of employment.

As the cryolite workers were exposed to high concentrations of fluoride dust but to no other suspected carcinogen during their employment, heavy respiratory exposure to fluoride could have contributed to the increased cancer risk observed. The potential role of fluoride in the causation of bladder cancer therefore needs to be explored.

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<sup>1</sup> Extended abstract of a report published in the journal of the National Cancer Institute.

<sup>2</sup> Institute of Community Health, Odense University, Denmark.

<sup>3</sup> Danish Cancer Registry, Danish Cancer Society, Copenhagen, Denmark.

<sup>4</sup> Danish Institute for Clinical Epidemiology, Copenhagen, Denmark.

Address for correspondence: Professor P. Grandjean, Odense Universitet, Institut for Sygdomsforebyggelse og Helsetjenesteforskning, Miljømedicin, Winsløwparken 17, DK-5000 Odense C, Denmark.

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